February 21, 1953

Dear Luca:

Your letter of the 8-10th arrived here yesterday, just after I got back to Madison. This is only a partial reply, concerning those matters that seem to demand the promptest attention.

1) Distribution of Hfr. My own inclination would still be to reserve the strain. Nelson is examining the point of the inhibition of recombination activity with drugs. Once the strain is released, it will be impossible to restrict its further distribution or application. My basic reasons are less rational however, namely that I have wished to preserve a protected climate so that we could proceed, for the time being without having to be concerned about the competitive activities of others. If Hayes has an Hfr of his own, that is all to the better as far as his own program is concerned, and I have no regret about that, but I just don't want to be a party to his work. He has already demonstrated his capacity for premature and irresponsible publication which may perhaps outbalance his constructive contributions. However, I will not insist on binding you to my own views, if you feel that it would be better from your own point of view to collaborate more closely with Hayes and to distribute these strains.

2) I will send you the strains requested at the earliest opportunity (H313; W-1678). The latter is F+; have I indicated otherwise? F+ from coli Waksman (our line 35) has been unstable in the K-12 line (line 1) in the few cases tasted. I will endeavour to do the F^r x F^r expts. suggested.

3) Thank you for arranging to send the Bolletino and Atti.... They have arrived in good condition and will permit our library to make up a complete set. as far as I good learn from the Bolletino with my limited ability in Italian, the 1st Congresso must have been purely a business meeting so that the Atti begin with the 2d Congresso. The library did, in fact, have several issues here and there, but these were never bound for lack of a complete set. Do you wish to give me any instructions concerning the surplusage? I will be glad to keep them for a couple of years, and send them on to anyone else who may ask for them, or to return them.

4) I learned recently of the CSH program myself, and have been invited to participate in the discussion. However, the program seems to have been arranged at Delbruck's caprice, despite its concern with the topic "Viruses". This is the only reason I can imagine why Hayes was invited, while, for example Boyd was not. I have not definitely decided whether we shall, in fact, attend as there are enough other things to worry about this summer. Whether we will be at the Congresses is still unsettled also.

5) It will take me a little time to get another sintered glass filter, but I will be delighted to do so. Would it be all right to send you only the filter and let your glass-blower make the U-tube (for which I will give specifications?) This would make shipment easier, cheaper and safer. If this would not be convenient for you, I will send the whole tube.

~~the you referring to W-1578 = H-Gal-Lac-F-~~ (the original of Hes. I's)
~~W-1678 = P-G-F+ λ^s~~ see over

6) I should be interested to hear from Dr. Calef directly if he is interested to work with me. I do not think I would have the energy to look after anyone who did not already have a fair background in bacterial genetics technique as well as a working command of English. Space is always relative: whether to take this fellow, or that one, or another graduate student. In fact, I would like to have someone work with me on Salmonella genetics so that I might have more time to spend on the K-12 cytology. Can you write me a little more detail about his experience, ability and background so that I could try to predict how well he might fit into our program? If Buzzati also sponsors him, I suppose he must be quite capable.

7) The question of the Chain-Symposium still troubles me. If you were not invited, despite Eagle's recommendation, it must be only to avoid having Italian nationals on a program to be held in Italy. Eagle insists that Chain could have no objection to a joint paper, so I assume we need consider only our own inclinations. I shall be very embarrassed to have to give such a paper without your collaboration. May I ask again that you do this, and confirm your decision by forwarding the enclosed letter to Chain with your views. Your paper which appeared in the WHO Bull. seems an excellent starting point, and I would suggest that we merely bring this up to date, perhaps condensing some of it to make room. If you wish, you would not have to spend any more time on it than to criticize the plastic surgery that I would suggest, though I would of course prefer as full a participation on your part as you have time to arrange.

8) We have been paying special attention to the occurrence of saturation in Hfr x F- crosses. That is, in buffer suspensions, the number of recombinants increases up to a certain point, with time, and then remains constant. Experiments with varying numbers of Hfr and F- cells suggest that one or the other parent can be limiting, and that at the time of saturation only about 10^{-3} of the less numerous parent have been able to react. This loss of competence has been verified by adding additional marked Hfr cells to the crosses; when the F- parent is more numerous, the marker appears in the progeny when the Hfr was more numerous, the F- parent is assumed to have become exhausted, as the added marker does not appear. A similar phenomenon may occur in crosses in broth, but is obscured by the continuous growth. It seems necessary to postulate a reaction of Hfr x F- which leads to incompetent cells (perhaps undetected recombinants??), as the initial rate of formation of recombinants greatly exceeds the calculated collision frequency if less than 10^{-3} of each parent is assumed competent. Superimposed on this, however, there is a decay of competence in the parents kept alone in buffer which is evidently slower than in the crosses. This seems to involve mostly the Hfr parent; it is accelerated by aeration, and somewhat resembles the F- phenocopy in aerated 58-161. Trials at different cell densities may help determine whether an Hfr-Hfr reaction is somehow involved. I am hoping, however, to redirect these experiments to the more pragmatic end of establishing the optimal conditions for microscopic study.

9) If as you mention you plan to write more extensively on the adsorption experiments, I will defer further discussion till then. I hope by then to be sufficently composed to give it more useful attention than immediate distractions will permit at the moment.

Yours sincerely,

Joshua Lederberg

* There is some confusion here.

W1578 = M- Lac_1- Gal_4- λ^s F- , Mrs. L.'s original sterile culture (W1607 = 1578S*)

You should already have this or the equivalent.

W1678 = P- G- F+ (not F-) I wish we did have an F-.

I assume this is what you want.

Dear Linda:

Your letter of the 6-10th arrived here yesterday, just after I got back to Madison. This is only a partial reply, concerning those matters that seem to demand the prompt test attention.